IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No.: 2895
DeGRADO *et al.*	Art Unit: 1627
Application No.: 10/801,951	
(Appeal No.: 2010-005832)	Examiner: CHONG, Yong Soo
Filed: March 17, 2004	Atty. Docket: 1694.0630003/JMC/M-R
For: **Facially Amphiphilic Polymers and Oligomers and Uses Thereof**	

Response to Order for Further Briefing

Board of Patent Appeals and Interferences
US Patent and Trademark Office
PO Box 1450
Alexandria, VA 22313-1450

Sir:

The Board of Patent Appeals and Interferences ("the Board") mailed an Order for Further Briefing on May 9, 2011. After petitioning for and receiving an extension of time to respond, Applicants hereby timely file one copy of this Response to the Board's Order.

It is not believed that further extensions of time are required beyond those already received. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned for. It is not believed that any additional fees beyond those accompanying this Response are required; but if they are, they are hereby authorized to be charged to our Deposit Account No. 19-0036.

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INTRODUCTION

Before the Board is the Applicants' appeal of the Examiner's final rejection of claims 16-48 and 67-73 for judicially created, nonstatutory obviousness-type double patenting. The matter has been fully briefed and is awaiting decision. On May 9, 2011, the Board issued an Order for Further Briefing ("Order") that required Applicants to brief two questions not previously before the Board:

1. "Whether Applicants may be required to restrict their claims to a single invention under the provisions of 35 U.S.C. § 121;" and

2. "Whether Claim 16 is a proper 'Markush Claim.'"[1]

(Order at 2.) Applicants address each question *seriatim.*

SECTION 121 QUESTIONS

In the Discussion section of the Order, the Board explained its Section 121 questions in more detail, stating:

1. "We require that Applicants brief the apparent conflict between the plain language of § 121 and the *Weber* and *Haas* opinions;" and

2. "[A]pplicants are required to address whether the language of the second paragraph of § 112, requiring 'one or more claims . . . claiming the subject matter the applicant regards as his invention' necessarily precludes the Director from exercising his statutory discretion 'to require the application to be restricted to one of the inventions' when more than one

[1]The Order is confusing because the Board, in certain sections, requests briefing only as to whether claim 16 is a proper Markush claim (Order at 2 & 12), while elsewhere the Board requests briefing on whether claims 16-48 are proper Markush groups. (Order at 11.) Applicants have addressed the broader question whether claims 16-48 are proper Markush groups.

Despite the Board's grouping of claims 16-48, Applicants' position is that claims 16-48 do not stand or fall together. Instead, because the determination as to whether a claim is a proper Markush group is decided on a case-by-case basis, each claim should be considered individually. *See In re Harnisch*, 631 F.2d 716, 722 (C.C.P.A. 1980). Therefore, each of claims 16-48 should be considered separately.

independent and distinct inventions are encompassed within a single claim."

(Order at 10-11.)

I. Summary of Responses to Section 121 Questions

Before responding to the two questions presented by the Board about the effect of Section 121 on the Director's ability to restrict claims, Applicants first will demonstrate that the Board has no jurisdiction to review a restriction requirement in this case and that it does not have the authority to require restriction *sua sponte*. Indeed, the Board's requirement that Applicants brief these issues is beyond the scope of 37 C.F.R. § 41.50(d), which only permits the Board to require additional briefing where the issue briefed may aid in a decision of the Board on the merits. Because the Board cannot reach the question of a restriction requirement in this case, briefing on Section 121 restriction issues cannot aid in the Board's decision on the merits of this appeal involving an obviousness-type double-patenting rejection. Second, Applicants will address the Board's first question on Section 121 and show that there is no conflict, apparent or otherwise, between Section 121 and the holdings in the *Weber* and *Haas* cases because *Weber* and *Haas* addressed the very meaning of Section 121 and are the controlling precedents. Third, Applicants will address the Board's second question on Section 121 and show that the second paragraph of Section 112, read together with Section 121, does not provide the Director with any discretion to require restriction within a single claim.

II. The Board Lacks Jurisdiction to Raise a Restriction Requirement Under Section 121 in This Case

The Board's action raises serious jurisdictional issues. The law to be applied to the facts of this matter is clear: the Board has no authority to raise a restriction requirement between claims in this case. *In re Watkinson*, 900 F.2d 230, 233 (Fed. Cir. 1990); *In re Hengehold*, 440 F.2d 1395, 1404 (Fed. Cir. 1971). Nor, under *Weber* and *Haas*, does it have the authority *sua sponte* to require restriction within a single claim. *In re Weber*, 580 F.2d 455, 458 (C.C.P.A. 1978); *In re Haas*, 580 F.2d 461, 464 (C.C.P.A. 1978).

Both the Federal Circuit and the Court of Customs and Patent Appeals ("CCPA") have held that the Board's jurisdiction is limited to the review of "adverse decisions" under 35 U.S.C. § 6 (previously 35 U.S.C. § 7). *Watkinson*, 900 F.2d at 233; *Hengehold*, 440 F.2d at 1404. Restriction requirements restricting *between claims* under Section 121 are not "adverse decisions" but are discretionary matters for the examiner. *Id.* As such, the Board has no authority to review challenges to restriction requirements between claims. Those challenges are instead properly petitionable to the Director. And where an examiner attempts to restrict *within a single* claim, and that decision is challenged on appeal by the applicant, the Board would have no discretion to do anything but reverse the decision under *Weber* and *Haas*, and under the plain language of Sections 121 and 112, second paragraph. Neither of these scenarios are present in this case. Instead, this case involves the Board raising a restriction issue that is not before it *sua sponte*; however, the Board has no such authority to raise that issue in this case.

The procedural posture of the restriction requirement is explained in detail *infra* in Sections IV.A.4 and IV.A.5 addressing the Markush questions. To summarize, the Examiner twice required restriction within claim 16. The second restriction within claim 16 was made final. In response to the second restriction of claim 16, Applicants elected a Group, amended claim 16 to expedite prosecution and traversed the restriction requirement. The Examiner made the restriction final but then exercised his discretion to withdraw the restriction requirement and proceeded to examine the full scope of amended claims 16-48. Thus, the Examiner withdrew the restriction requirement at least with respect to presently pending claim 16. Accordingly, by the time of this appeal, there was no case or controversy regarding claim restriction.

What the Board appears to seek by requiring this supplemental briefing is justification for itself to review the prosecution history below and, *sua sponte*, require the applicant to restrict within a single claim or among claims. The sole authority under which the Board seeks this supplemental briefing is 37 C.F.R. § 41.50(d). While the Board has broad authority under 37 C.F.R. § 41.50 to review examiner *decisions*, including the authority to issue new grounds of rejection, that authority never extends to *sua sponte*

review of restriction requirements. Rule 41.50(d) only allows the Board to require an appellant to provide additional briefing on an issue that "the Board considers to be of assistance in reaching a reasoned decision on the pending appeal." And the only decision presented to the Board in this appeal was the judicially created obviousness-type double-patenting rejection. The Board thus cannot rely on Rule 41.50(d) to provide it jurisdiction or authority to act in this case.

Because, in this case, Applicants have not presented any issues to the Board that deal with restriction, the Board has no authority under its own rules to review restriction requirements here. And even if it did, *Hengehold* and *Watkinson*, read together, and *Weber* and *Haas*, read together, restrict its ability to act. For these reasons, additional briefing on a restriction issue that is not before the Board in this appeal cannot have any bearing on the Board reaching a reasoned decision on the single issue that was actually presented in this appeal: the judicially created obviousness-type double-patenting rejection. The Board's Order requiring briefing on Section 121 restriction issue is therefore beyond the Board's authority under the Patent and Trademark Office ("Office") rules; and thus, there is no jurisdictional basis for the Board even to pose these questions.

III. There Is No Conflict between Section 121 and the Weber *and* Haas *Decisions*

The Board asked Applicants to brief the "apparent conflict" between the plain language of Section 121 and *Weber* and *Haas*. (Order at 10.) The Board's framing of the question suggests the Board views the CCPA's opinions as wrongly decided.

Applicants do not agree that there is a conflict between Section 121 and the *Weber* and *Haas* decisions or that the CCPA wrongly decided these cases. In *Weber* and *Haas*, the CCPA interpreted the plain language of Section 121, and as the Board correctly stated in the Order, the CCPA in *Weber*, 580 F.2d at 458 held that the Director cannot require a restriction of a single claim because the plain language of Section 121 does not provide a separate basis for the Director to reject a claim. (Order at 10-11.) The CCPA in *Haas*, decided the same day as *Weber*, favorably cited *Weber* for the proposition that Section 121 does not provide a basis to reject a claim. *Haas*, 580 F.2d at 464. Simply put, there is no

conflict between the *Weber* and *Haas* decisions and Section 121 because those cases hold, after providing a thorough analysis of the plain language of Section 121, what the plain language of Section 121 means. Significantly, both *Weber* and *Haas* remain good law; the Federal Circuit has never revisited these holdings. Accordingly, there is no conflict, and the Board remains legally bound by those cases.

The holding that Section 121 does not permit the Director to require restriction with a single claim is fully consistent with the long-established principle that the claims define the invention. *See e.g. Johnson & Johnston Assoc. Inc. v. R.E. Serv. Co.*, 285 F.3d 1046, 1052 (Fed. Cir. 2002) ("Consistent with its scope, definition, and notice functions, the claim requirement presupposes that a patent applicant defines his invention in the claims, not in the specification. After all, the claims, not the specification, provide the measure of the patentee's right to exclude.") A single claim cannot be considered "two or more independent and distinct inventions" because the claim is the invention, as determined by the inventors. This proposition was recognized by the CCPA in *Weber* and *Haas*. *Weber*, 580 F.2d at 458; *Haas*, 580 F.2d at 464.

IV. The Director Has No Discretion to Restrict Within a Single Claim Under Section 112, Second Paragraph

In its second Section 121 question, the Board asked whether Section 112, second paragraph, precludes the Director from exercising his statutory authority to restrict an application to one invention when a single claim contains one or more inventions. (Order at 11.) As with its first question, by including the phrase "when a single claim contains one or more inventions," the Board shows its displeasure with *Weber* and *Haas*. However, the Board's characterization does not affect the answer.

The plain language of Section 112, second paragraph, as recognized by the courts, removes all discretion from the Director to restrict within a single claim. Again, *Weber* is controlling. *Weber* indicates that the Director has no discretion to require a restriction within a single claim. 580 F.2d at 455. The CCPA based this holding on two grounds. First, the plain language of Section 121 does not grant the Director any discretion to require restriction of a single claim: "It is apparent that § 121 provides the Commissioner with the

authority to promulgate rules designed to restrict an application to one of several *claimed inventions* when those inventions are found to be 'independent and distinct.' It does not, however, provide a basis for an examiner acting under the authority of the Commissioner *to reject a particular claim on that same basis*." *Id.* (emphasis added). That is, Section 121 permits an application with multiple claims to be restricted between claims, but a single claim cannot be so restricted.

Second, the plain language of Section 112, second paragraph, does not provide the Director with any discretion to require a restriction within a single claim. That section specifically gives the applicant the sole right to define the invention, stating:"[t]he specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which *the applicant* regards as his invention." 35 U.S.C. § 112, second paragraph (emphasis added). The proper scope of invention is thus what the applicant regards as his invention, not what the examiner regards as the invention. The court in *Weber* could not have been more clear:

> An applicant is given, by the statute, the right to claim his invention with the limitations he regards as necessary to circumscribe that invention, with the proviso that the application comply with the requirements of § 112. We have decided in the past that § 112, second paragraph, which says in part "(t)he specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention," allows the inventor to claim the invention as he contemplates it. *In re Wolfrum*, 486 F.2d 588, 179 USPQ 620 (CCPA 1973).
>
> As a general proposition, an applicant has a right to have each claim examined on the merits. If an applicant submits a number of claims, it may well be that pursuant to a proper restriction requirement, those claims will be dispersed to a number of applications. Such action would not affect the right of the applicant eventually to have each of the claims examined in the form he considers to best define his invention. If, however, a single claim is required to be divided up and presented in several applications, that claim would never be considered on its merits. The totality of the resulting fragmentary claims would not necessarily be the equivalent of

> the original claim. Further, since the subgenera would be defined by the examiner rather than by the applicant, it is not inconceivable that a number of the fragments would not be described in the specification.

Weber, 580 F.2d at 458.

Finally, the *Weber* court recognized the Office's need to be able to manage examiner workloads and the searching done per patent application filed. But the CCPA held the applicant's statutory right to claim his invention as he saw fit under Section 112 trumped the administrative interests of the Office.[2] *Id.*

V. Conclusion With Respect to Section 121 Questions

The Board poses important questions dealing with restriction practice in the chemical and biological arts. Indeed, the importance of the issues is well reflected in the prosecution to date of the pioneering inventions disclosed and claimed in the present application. But under the current state of the law, the questions are simply outside the Board's statutory and regulatory jurisdiction.

Applicants now turn to the Board's questions surrounding proper Markush claiming.

MARKUSH QUESTIONS

In the Discussion section of the Order, the Board explained its Markush claims questions in more detail, stating:

> 1. "Applicants are required to brief whether the recitation of a broad general formula covering a very large group of compounds, the recitation of a general chemical property (amphiphilicity) that may be possessed by those compounds, and the recitation of the single broad step of 'administering an effective amount' is per se sufficient to create 'unity of invention' as that concept was used by the *Harnisch* court;" and

[2]In footnote 8 of *Weber,* the CCPA suggested that the Office could use its statutory fee-setting authority to address its administrative burdens.

2. "Applicants are also required to brief whether, considering only the oligomers as defined by Formula II in Claim 16, the 21 groups identified by the Examiner are unrelated inventions. Stated another way, do those groups share any additional structural or functional features that would establish unity of invention?"

(Order at 12.)

I. Summary of Responses to Markush Questions

The Applicants will address the two questions presented by the Board. But first, just as with the Applicants' response to the Board's Section 121 questions, Applicants first will show that the Office has no statutory basis for "rejecting" claims as having an improper Markush group. Turning to the Board's two Markush questions, Applicants will demonstrate that there is no *per se* rule governing unity of invention; nor should there be. Applicants then turn to the substantive issue of whether claim 16 meets the tests applied for determining unity of invention. Within that section, Applicants will demonstrate that Applicants' claims meet the tests established by *Harnisch*, *Hozumi*, and the PCT. Finally, Applicants will address the sound public policy behind allowing Applicants, not the Office, to set forth the metes and bounds of what Applicants regard as their invention, especially for the type of important pioneering inventions disclosed and claimed in the present application.

II. The Office Has No Statutory Basis For Rejecting the Claims

First, the Office has no statutory basis for rejecting claims 16-48 as having an improper Markush group. The Office cannot accomplish indirectly, by asserting an improper Markush grouping, what it cannot accomplish directly under Section 121. Specifically, in *Weber* and *Haas*, the CCPA held that the Office cannot reject a claim under 35 U.S.C. § 121 as being an improper Markush claim. *Weber*, 580 F.2d at 459; *Haas*, 580 F.2d at 464. Additionally, the CCPA held in *Wolfrum* that the Office cannot reject a claim under 35 U.S.C. § 112, second paragraph, as encompassing an improper Markush group. *Wolfrum*, 486 F.2d at 591.

The Federal Circuit has stated that under *Weber* and *Haas*, it is "never proper for an examiner to reject a Markush claim under 35 U.S.C. § 121," noting that "the rejection of a Markush claim is different from a restriction requirement between different claims." *Watkinson*, 900 F.3d at 233 (citations omitted). Even though in *Harnisch* the CCPA found that the claim was a proper Markush claim, the CCPA, in *dicta,* suggested the Office can reject a claim as being an improper Markush group. 631 F.2d 716, 722 (C.C.P.A. 1980). The CCPA did not address whether the Office can reject a claim as being an improper Markush group or provide a mechanism by which the Office can reject the claim. *Id.* In fact, Applicants are not aware of any CCPA or Federal Circuit case holding a claim invalid for an improper Markush group, and the Federal Circuit's finding in *Watkinson* has supplanted the *dicta* in any event.

Even if the Office has the right to reject claims 16-48 for containing an improper Markush group, a review of the facts shows, when applying the proper standards, that the amphiphilic, antimicrobial compounds for use in the recited methods of claims 16-48 all have unity of invention and therefore are proper Markush groups.

III. There Is No Per Se *Rule in Determining a Proper Markush Group*

The Board has required the Applicants to brief whether the "recitation of a broad general formula covering a very large group of compounds, the recitation of a general chemical property (amphiphilicity) that may be possessed by those compounds, and the recitation of a single broad step of 'administering an effective amount' is per se sufficient to create 'unity of invention' as that concept was used by the *Harnisch* court." (Order at 12.)

The Board's Order frames the Markush issue as whether there is a *per se* rule for determining unity of invention as that concept was used by the *Harnisch* court. The CCPA has answered that question, rejecting the application of any *per se* test, stating that whether a Markush group is improper must be decided on a case-by-case basis. *Harnisch*, 631 F.2d at 722. The test is a highly fact-intensive analysis of whether the "compounds [that] all belong to a subgenus, as defined by [applicant], . . . is not repugnant to principles of scientific classification." *Id.* The resolution of this issue must be based on the facts presented.

Therefore, there is no *per se* rule for determining unity of invention. *See also Ex parte Gante*, 2004 WL 77420 (Bd. Pat. App. & Interf. 2004) (unpublished)(Senior Administrative Patent Judge McKelvey vacated an "improper Markush rejection" and remanded for further fact-finding, noting that "[e]ach case is decided on its own facts and necessarily involves the exercise of reasoned discretion.")

To support its *per se* question, the Board asserts that the claimed formula is broad and covers a "very large group of compounds," "estimating that claim 16 covers 400 billion compounds. (Order at 5& 12.) The Board's attempt to prejudice the answer misses the point. The breadth of the formula and number of compounds are not relevant to deciding whether a Markush claim is proper.

The Office's practice in granting chemical patents is proof that there is no *per se* rule tied to the number of compounds claimed. The Office has issued patents with claims encompassing more compounds than claim 16. For example, U.S. Patent Nos. 7,678,801 (Exhibit A); 7,825,216 (Exhibit B); 7,897,596 (Exhibit C); 7,932,242 (Exhibit D); and 7,939,553 (Exhibit E) all have claims that encompass more than 400 billion compounds. A conservative estimate of the number of compounds encompassed by each patent is as follows: greater than 10^{21} compounds (Exhibit A, claim 1); greater than 10^{41} compounds (Exhibit B, claim 1); greater than 10^{35} compounds (Exhibit C, claim 1); greater than 10^{36} compounds (Exhibit D, claim 1); and greater than 10^{106} compounds (Exhibit E, claim 1). Examiners routinely examine the scope of such claims. Furthermore, Judge Rich's concurrence in *Weber* demonstrates there is no *per se* rule, because there is "no excuse at all for refusing to examine a broad generic claim - no matter how broad, which means no matter how many independently patentable inventions may fall within it." *Weber*, 580 F.2d at 461. Therefore, the breadth of the claim is irrelevant to the analysis of whether a claim contains a proper Markush group.

As described *infra* in Section IVA, although the Examiner initially issued a restriction requirement dividing the scope of claims 16-48 into twenty-one (21) different groups, the Examiner ultimately examined the full scope of the currently pending claims.

(Office Action, March 29, 2007, pp. 2-3; Office Action, October 30, 2007, p. 2.) Because the Examiner indicated that he searched the full scope of claims 16-48 and because the search notes do not evidence an undue amount of searching, the Examiner must not have found the search unduly burdensome.

Furthermore, Applicants could have drafted a true "generic" claim without using a Markush group. In that event, the scope of such a claim would have been broader than that of claims 16-48, potentially of infinite scope. The Examiner would have had to search the full scope of the presented generic claim. This type of claim and searching are routine in the electrical and mechanical arts. Thus, examiners routinely examine claim scopes broader than those of claims 16-48. For this additional reason, the breadth of the claim is irrelevant to the analysis of whether a claim contains a proper Markush group.

That said, as set forth below, a claim reciting (1) a general chemical formula having a common structure, (2) a chemical property possessed by the group of claimed compounds, and (3) the step of administering an effective amount of one of the claimed compounds would possess unity of invention as stated in *Harnisch*.

IV. Claims 16-48 Contain Proper Markush Groups Because the Groups Possess Unity of Invention

The second question Applicants have to address pursuant to the Order relates to whether the twenty-one (21) groups identified by the Examiner are unrelated inventions—are the pending claims proper Markush claims. (Order at 11.) Answering that question, which was resolved during prosecution and therefore should be a moot issue, is a fact-intensive exercise. Applicants did not appeal that issue to the Board. For these reasons, in advance of addressing whether the claims are proper Markush claims, Applicants provide the following Statement of Facts to provide proper context for their response.

A. Statement of Facts in Support of Markush Arguments

1. Status of Claims

Claims 16-48 and 67-73 are pending and rejected under the judicially created doctrine of obviousness-type double patenting. Claims 1, 15, 49, 54-56, 62, 63, 65, and 66 are pending and withdrawn as being directed to nonelected claims. Claims 2-14, 50-53, 57-60, 61, and 64 were cancelled.

2. Summary of Claimed Subject Matter

Applicants' invention, as defined by independent claim 16, is generally directed to a method of treating a microbial infection in an animal in need thereof comprising administering to the animal an effective amount of a pharmaceutical composition comprising a pharmaceutically acceptable carrier or diluents and an amphiphilic oligomer of general Formula II: R^1-[x-A_1-x-y-A_2-y-]$_m$-R^2 or an acceptable salt or solvate thereof. The repeating subunit of the oligomers of Formula II contain an amide bond (-NH-C(=O)) linking two aromatic rings. Additionally, the oligomers of Formula II are amphiphilic—they have a hydrophobic face and a hydrophilic face.

3. Brief Description of the Invention

The invention was previously described in Applicants' Appeal Brief filed September 23, 2009. The following discussion is provided to address the Board's questions set forth in the Order. The application discloses, *inter alia*, "methods of using facially amphiphilic polymers and oligomers, including pharmaceutical uses of the polymers and oligomers as antimicrobial agents and as antidotes for hemorrhagic complications associated with heparin therapy." (Specification, p. 1, para. [0002].)

(a) The Subject Matter of the Application is a Pioneering Technology

According to the specification, the antimicrobial amphiphilic oligomers utilized in the claimed methods were based upon proprietary computational computer-modeling technology. (*See* specification, p. 109, para. [0270].) The technique developed by the inventors for designing active compounds is different than that traditionally used in the

industry, which involves making only minor modifications to known compounds. (Exhibit F, p. 4, para. 8.) The proprietary computer modeling provides an innovative technique to develop compounds having a common structure, such as a common secondary or tertiary structure, for a common activity.

This application is assigned to the Trustees of the University of Pennsylvania ("UPenn"). UPenn has exclusively licensed this application to PolyMedix, Inc. ("PolyMedix") (*Id.*, p. 2, para. 5.) PolyMedix has utilized the proprietary technology disclosed in this application to develop lead compounds that are currently in clinical trials. (*Id.*, pp. 1-2, paras. 2-3; & p. 11, paras. 13-14.) Currently, PolyMedix also is investigating a large number of amphiphilic oligomers for antimicrobial, antiviral, antifungal, and anti-heparin activity. (*Id.*, p. 3, para. 7; & p. 13, para. 20.)

(b) Naturally Occurring Antimicrobial Peptides Have a Common Structure

The specification teaches that naturally occurring host defense peptides possess bactericidal, antifungal and/or antiviral activity. (Specification, pp. 2-6, para. [0004]-[0013].) Additionally, the specification discloses that these peptides, although composed of different primary amino acid sequences, share remarkably similar physicochemical properties. (Specification, p. 5, para. [0013].) The peptides "adopt an amphiphilic architecture with positively charged groups segregated to one side of the secondary structure and hydrophobic groups on the opposite surface." (*Id.*) In fact, it is the overall physiochemical properties that are responsible for the biological activity of these peptides and not the precise amino acid sequence. (Specification, p. 6, para [0013].)

The inventors made the following observation regarding naturally occurring host defense peptides:

> [F]acial amphiphilicity, *i.e.,* the alignment of polar (hydrophilic) and nonpolar (hydrophobic) side chains on opposite faces of a secondary structural element formed by the peptide backbone, and not amino acid sequence or any particular secondary/tertiary structure, chirality or receptor specificity, is responsible for the biological activity of these peptides.

(Specification, p. 6, para. [0013].)

The specification reports that "investigators have designed synthetic antimicrobial peptides by idealizing the amphiphilic α-helical arrangement of sidechains observed in the natural host defense peptides, leading to a large number of potent and selective antimicrobial compounds." (Specification, p. 6, para. [0014].)

(c) Antimicrobial Oligomers of the Claimed Invention Have a Common Structure

Based upon the observations described above and other insights, the inventors arrived at a series of synthetic molecules (oligomers and polymers) designed to have antimicrobial activity and to be amphiphilic—that is the alignment of polar (hydrophilic) and nonpolar (hydrophobic) side chains on opposite faces. Amphiphilicity is related to the secondary and tertiary structure of the oligomers and polymers of Formulae I to XX. This common amphiphilicity structure is the mechanism by which the compounds exhibit antimicrobial activity. The primary structure of the backbones and selection of appropriate sidechains provides the amphiphilic structure of the oligomers and polymers of the claimed invention.

The inventors designed various synthetic oligomers having polar and nonpolar faces as antimicrobial, antifungal, and/or antiviral agents. (Specification, p. 15, para. [0059].) The goal of the synthetic approach was to capture the structural and biological properties of antimicrobial peptides within the framework of inexpensive oligomers. (*Id.*) While previous molecules had been developed that solved some relatively simple problems such as susceptibility to proteolysis, more severe problems associated with these earlier molecules have included the expense of the materials, toxicity, limited efficacy, and limited tissue distribution. (*Id.*) Particularly, the specification discloses that, "non-peptidic mimetics are significantly smaller and easier to prepare than their naturally occurring counterparts . . . are significantly less toxic towards human erythrocytes, much less expensive to prepare, and are expected to be much more stable *in vivo*." (Specification, p. 15, para. [0059].) Therefore, the specification discloses that the oligomers and polymers of the invention are easier to make and are less toxic than the naturally occurring peptides.

The oligomers useful in the claimed invention mimic the structure of naturally occurring peptides. (Specification, p. 15, [0059].) "[B]ecause these compounds mimic the structure and biological activity of host defense peptides, the appearance of bacterial resistant strains is very unlikely to occur." (*Id.*) Therefore, the inventors reasoned that small synthetic oligomers that adopt amphiphilic secondary structures while exhibiting potent and selective antimicrobial activity would be less expensive to produce, would have better tissue distribution, and would be easier to fine-tune their structures and activities to minimize toxicity.

In describing how to carry out the invention, the specification discloses that in one embodiment,

> [f]acially amphiphilic polymers and oligomers of the present invention can be homopolymers wherein one monomer is substituted, with both a nonpolar and a polar substituent or copolymers wherein one monomer is substituted with a polar substituent and the other monomer is substituted with a nonpolar substituent. Since the antimicrobial activity arises from the amphiphilic character conferred by a periodic pattern of side chains rather than the precise spatial arrangement of side chains, other substitution patterns are also expected to produce facially amphiphilic polymers and oligomers and they all are encompassed by the present invention.

(Specification, p. 17, para. [0066].)

4. Relevant Portions of the File History

On April 10, 2006, the Examiner issued a first restriction requirement and a requirement for species election, requiring division of the claims into fifteen (15) separate inventions I-XV, and requesting election of a single species. (Restriction Requirement, April 10, 2006, pp. 2-3). The Examiner divided the fifteen (15) alleged inventions based on method of use (*e.g.*, treating a microbial infection and providing an antidote) and Formula (*e.g.*, Formula I and Formula II). (*Id.*) The Examiner asserted that "[t]he inventions are distinct," and that "Inventions I-XIV are unrelated." (*Id.* at p. 3-4.)

On June 12, 2006, Applicants elected Group III drawn to a method of treating a microbial infection in an animal, the method comprising administering an effective amount

of a pharmaceutical composition comprising an oligomer of Formula II. (Reply to Restriction Requirement, June 12, 2006, p. 2.) The election was made without prejudice to or disclaimer of the other claims or inventions disclosed. (*Id.*) Applicants provisionally elected an oligomer of Formula II with traverse. (*Id.* at pp. 2-3.) Applicants traversed the rejection by arguing that the Office should search and examine Group IV along with Group III because the claims of Group IV defined a sub-genus entirely encompassed within the scope of claim 16 in Group III. (*Id.*)

On September 6, 2006, the Examiner issued a second restriction requirement, requiring restriction under 35 U.S.C. § 121 within a single claim. (Restriction Requirement, September 6, 2006, pp. 2-5.) The Examiner required restriction of the previously elected Group III claims to one of twenty-eight (28) separate groups, Groups I-XXVIII. Group I is illustrative:

> Claims 16-48 (in part) are drawn to a method of treating a microbial infection in an animal comprising administering an oligomer of Formula II, where x and y are taken together to be an amide, and A1 and A2 are independently arylene substituted with non-polar groups, classified in 514/675.

(*Id.* at p. 2.)

Applicants replied on October 24, 2006, amending claims 16, 49, and 50 to require administering an amphiphilic oligomer. (Amendment and Reply, October 24, 2006, pp. 10, 21, & 24.) "[T]he group that encompasses the species oligomer of Formula II previously elected" was provisionally elected. (*Id.* at p. 51.) However, Applicants traversed the election requirement because "Applicants cannot determine which group to elect because the previously-elected oligomer does not fall within the scope of any of the twenty-eight restriction groups listed in the present Restriction Requirement." (*Id.* at p. 54.) Additionally, Applicants stated that "Applicants would elect one of the oligomers of Formula II listed on pages 100-105 of the specification, but again none of these oligomers appear to fall within the scope of any of the twenty-eight restriction groups listed in the present Restriction Requirement . . . ." (*Id.*) Applicants further indicated that none "of the individual oligomers of Formula II disclosed throughout the entire specification appear to fall within the scope of any of the twenty-eight restriction groups . . . . " (*Id.* at pp. 51-52.)

Applicants also argued that the Office had no authority to restrict within a single claim. (*Id.* at p. 54.)

On December 28, 2006, the Examiner issued a third restriction requirement, withdrawing the second restriction requirement. (Restriction Requirement, December 28, 2006, p. 2.) Applicants were required to elect one of twenty-one (21) allegedly separate groups within claim 16, Groups I-XXI, and make a species election. (*Id.* at pp. 2-5.) The Examiner contended that the inventions were unrelated because "[i]n the instant case, the different inventions are classified under several formulas, which may include multiple and various polar groups (PL), non-polar groups (NPL), heteroarylene groups, heteroatoms, as well as other functional groups, comprising oxygen, nitrogen, and sulfur." (*Id.* at p. 5.)

On January 29, 2007, Applicants elected Group III and elected a species with traverse. Applicants again argued that the Examiner had impermissibly restricted within a single claim, contrary to the holdings of *In re Weber* and *In re Haas*. (Reply to Restriction and Election of Species Requirement, January 29, 2007, p. 3.) Applicants also argued that the amphiphilic oligomers "all share the common structure of amphiphilicity and common utility of effectiveness in the claimed method." (*Id.* at p. 2.) Applicants further requested that the Group III claims be rejoined to the claims of Groups I and II because the groups were classified the same and presented no burden to search and examine together. (*Id.* at p. 3.)

In the subsequent Office Action dated March 29, 2007, the December 2006 restriction requirement was made final. (Office Action, March 29, 2007, p. 2.)

Applicants subsequently negotiated with the Examiner in an effort to advance prosecution and move beyond the restriction requirement. For example, an Examiner Interview Summary states that

> Applicant[s] is [sic] willing to narrow the scope of the claims around the species election, specifically around the amide linkage between x and y, and defining what the scope of heteroarylenes are. Applicant[s] also discussed that this invention is designed for administration to an animal as opposed to in vitro use.

(Examiner Interview Summary, May 21, 2007.)

Following the extensive exchange between Applicants and the Examiner regarding restriction, the Examiner withdrew the December 2006 restriction requirement and examined the full scope of the claims on the merits.

> Claim(s) 1-12, 15-51, 54-59, 62-63, [and] 65-68 are pending. Claim(s) 16 [and] 49-50 been amended. Claims 66-68 are new .... Claim(s) 16-48 [and] 67-68 are examined herein insofar as they read on the elected invention.
>
> The species election (last compound for claim 68) is free of the prior art. The search will now be broadened to the full scope of the claims as it reads on the elected invention.

(Office Action, March 29, 2007, pp. 2-3.)

In the following Office Action, the Examiner stated that the "Examiner reminds Applicant [sic] that as stated in the last Office Action, *the species requirement has been withdrawn*, therefore the full scope of the claims will be examined." (Office Action, October 30, 2007, p. 2)(emphasis added).

On August 20, 2007, Applicants amended claim 16 to narrow "x" and "y" in such a manner that "x-y" would include an amide bond. (Amendment and Reply, August 20, 2007, p. 42.)

A review of the electronic file wrapper does not show that the search and examination of the application imposed any serious burden on the Examiner. On August 28, 2006, the Office conducted an STN database search, which appears to have taken about half an hour. (Search Results dated August 28, 2006). On March 13, 2007, The Examiner conducted an EAST search using the US-PGPUB, USPAT, USOCR, EPO, JP and Derwent databases. The query included searching each inventor's last name, the words "microbial, injection, microorganism, amphiphilic, and the patent classes 528 (subclass 322), 424 (subclass 422)." It appears the Examiner found U.S. Patent 7,173,102 B2 as the only hit. The Search Notes state that "Inventor" was searched on EAST and PALM; "Text" was searched on EAST and STN.

The search of March 13, 2007, appears to have been updated on October 25, 2007. See the handwritten term "updated" on the paper. Additionally, there was a search of "Inventor and Text" on July 18, 2008, as well as a search of "Inventor and Text" on January 29, 2009, which appears to be a repetition of the July 18, 2008, search.

5. Clarification of the Facts Recited in the Order

The Board set forth a number of "facts" in the Order which require clarification. First, the Board states that "[t]he subject matter of Claim 16 relates to a method for treating microbial infections by administering any of a large variety of compositions. The compositions must include at least one amphiphilic oligomer." (Order at 2.) Claim 16 does not require simply administering an oligomer that is amphiphilic as suggested by the Board. Instead, claim 16 is directed to a method of treating a microbial infection in an animal in need thereof comprising administering to the animal an effective amount of a pharmaceutical composition comprising a pharmaceutically acceptable carrier or diluents and an amphiphilic oligomer that includes amide bond linking two aromatic rings. (Appeal Brief, p. 27.) Therefore, claims 16-48 require that (i) the oligomer be amphiphilic (*i.e.*, contains at least one polar and one nonpolar group), (ii) the oligomer contains a repeating core structure of two aromatic rings linked by an amide bond; and (iii) the oligomer be effective in treating a microbial infection in an animal in need of such treatment.

Second, the Board indicated that "[n]one of the original claims required that the oligomers be amphiphilic." (Order at 5.) That statement is contrary to the specification which explicitly states that "[t]he present invention relates to methods of using facially *amphiphilic oligomers* as antimicrobial agents and as antidotes for hemorrhagic complications associated with heparin therapy." (Specification, p. 1, para. [0002])(emphasis added). Therefore, the inventors intended that the compounds to be administered in the claimed methods be amphiphilic.

Third, the Board stated that "[u]pon initial review, an Examiner identified fifteen independent and distinct inventions (Groups I-XV) and required Applicants to elect one of them. The Examiner found that inventions I-XV were directed to unrelated inventions."

(Order at 5-6 (internal citations omitted).) However, as discussed above, the Examiner divided the fifteen (15) alleged inventions based on method of use (*e.g.*, treating a microbial infection and providing an antidote) and Formula (*e.g.*, Formula I and Formula II). (Restriction Requirement, April 10, 2006, pp. 2-3.) Additionally, the Examiner only asserted that inventions were distinct, not "independent and distinct," as incorrectly stated by the Board. (*Id.* at p. 2.)

Fourth, the Board indicated that "[t]he Examiner performed a preliminary search of the prior art and entered an additional restriction requirement for the Group III invention, Claims 16-48. He identified twenty-eight independent classes of oligomers." (Order at 6.) As described above, the Examiner's restriction requirement divided claim 16 into multiple alleged independent inventions. (Restriction Requirement, September 6, 2006, pp. 2-5.) However, as described above, none of the groups which the Examiner identified encompassed the compound the Applicants elected, much less any compound described in the specification. (Amendment and Reply, October 24, 2006, pp. 51-54.) Applicants also amended claims 16, 49 and 50 to more clearly define the Applicants' invention. (Amendment and Reply, October 24, 2006, pp. 10, 21, 24, & 52.)

Finally, the Board's Order never addressed the important fact that the Examiner subsequently withdrew the restriction requirement. As described above, the record clearly indicates that the Examiner withdrew the restriction requirement and examined the full scope of the claims. Thus, by October 30, 2007, no controversy existed between the Office and Applicants over the Examiner's previous attempts to restrict within any claim, including claim 16. The controversy was mooted by Applicants' voluntary amendment of claim 16 to require the repeating structure to include two aromatic rings linked by an amide bond, by the Examiner's statement at the outset of the Office Action that the full scope of the claims will be examined, and by the Examiner's action in examining the full scope of amended claim 16.

B. Currently Pending Claims 16-48 Are Proper Markush Claims

The Board required Applicants to brief whether the twenty-one (21) groups identified by the Examiner are unrelated inventions—that is, are the pending claims proper

Markush claims. However, after three restriction requirements, Applicants amended original claim 16 to encompass a smaller subset or subgenus of Formula II compounds than was recited in originally filed claim 16. Thus, currently pending claim 16 encompasses a much smaller genus, shaped partly as a result of the Examiner's three restriction requirements, than the broader invention the Board incorrectly describes.

The record clearly demonstrates that the Examiner withdrew the restriction requirement and examined the full scope of the claims. Thus, by October 30, 2007, no controversy existed between the Office and Applicants over restriction of claim 16. The controversy was mooted by Applicants' voluntary amendment of claim 16, the Examiner's statement at the outset of the Office Action that the full scope of the claims will be examined, and the Examiner's action in examining the full scope of amended claim 16. The Board's question ignores Applicants' amendments and the Examiner's withdrawal of the restriction requirement and subsequent reexamination of the full scope of the amended claims. Therefore, Applicants have addressed whether claims 16-48 on appeal include a proper Markush group.

1. The Compounds of the Methods of Claims 16-48 Meet the Test Established by **Harnisch** *that the Grouping of the Claimed Compounds is Not Repugnant to The Principles of Scientific Classification*

A proper Markush claim recites "compounds [that] all belong to a subgenus, as defined by [applicant], which is not repugnant to principles of scientific classification." *Harnisch,* 631 F.2d at 722. In *Harnisch,* the CCPA stated the claimed Markush group was not repugnant to the principles of scientific classification and therefore was not improper because the claimed compounds had a common structure and a common activity. *Harnisch,* 631 F.2d at 722. In *Harnisch,* the Office conceded that the claimed compounds contained a coumarin core and all functioned as dyes. *Id.* No CCPA or Federal Circuit decision has ever applied the *Harnisch* test and held that a Markush group was repugnant to principles of scientific classification.

The genus of compounds of Formula II required by the methods of claims 16-48 is not repugnant to the principles of scientific classification because the defined group possesses a common structure and a common function.

(a) The Compounds of Claims 16-48 Have a Common Structure

Applicants' claimed compounds have a common core structure, as well as a common secondary and tertiary structure.

Claims 16-48 require an amphiphilic compound of Formula II be administered in the recited uses. Formula II has the following structure: R^1-[A_1-x-y-A_2]$_m$-R^2. Claims 16-19, 22-24, and 26-47 require that A_1 and A_2 are *o*-, *m*-, or *p*-phenylene or heteroarylene. Claims 20, 21, 25, and 48 require that A_1 and A_2 be phenylene. Because phenylene and heteroarylene are examples of aromatic rings, the compounds all contain a repeating structure of two aromatic rings. (*See* Exhibit G; specification, pp. 23-24, paras. [0085], [0086], [0090], & [0091].) Additionally, because x is $-NR^8$, $-N(R^8)N(R^8)-$, or $-C(R^7R^7)NR^8-$, y is $-C(=O)$, and R^8 is hydrogen, the *x*-y linker between the aromatic rings contains an amide bond. Therefore, all of the compounds of claims 16-48 have a common repeating core structure of two aromatic rings connected by an amide bond.

Claims 16-48 also require that the administered compounds have antimicrobial activity. According to the specification, the "facial amphiphilicity, *i.e.*, the alignment of polar (hydrophilic) and nonpolar (hydrophobic) side chains on opposite faces of a secondary structural element formed by the peptide backbone, and not amino acid sequence or any particular secondary/tertiary structure, chirality or receptor specificity, is responsible for the biological activity of these peptides." (Specification, p. 6, para. [0013].) Therefore, to satisfy the antimicrobial activity requirement of claims 16-48, the polar and nonpolar substituent groups attached to the aromatic rings of the core structure must be on opposite faces of the molecule. Accordingly, the compounds of claims 16-48 have a repeating core structure of two aromatic rings connected by an amide bond, wherein the aromatic rings are substituted with polar and nonpolar substituent groups on opposite faces of the molecule. As such, the compounds of claims 16-48 have a common repeating core structure.

In addition to having a common repeating core structure, the compounds of claims 16-48 have a common secondary and tertiary structure. As described above, naturally occurring host defense peptides are amphiphilic and therefore have polar (hydrophilic) and nonpolar (hydrophobic) side chains on opposite faces of the peptide backbone. (Specification, p. 6, para. [0013].) According to Richard W. Scott, Ph.D., Vice President of Research at PolyMedix, the amphiphilicity of these naturally occurring host defense peptides results in a common secondary and tertiary structure. (Exhibit F, pp. 8-11, para. 12.)

The specification discloses that the oligomers of the invention were designed to mimic the amphiphilic structure of the naturally occurring host defense peptides. (Specification, p. 15, para. [0059].) Dr. Scott confirms that because the oligomers are amphiphilic, then the oligomers also have a common secondary and tertiary structure. (Exhibit F, pp. 8-11, para. 12.)

At the time the CCPA decided *Harnisch*, scientists focused on the primary structure of drug molecules. However, scientists are now focusing on secondary and tertiary structures of compounds to develop active drug molecules for a desired treatment. (Specification, pp. 12-13, para. [0046]-[0048]; p. 14, para. [0057]; p. 17-21, paras. [0066]-[0073] & Exhibit F, pp. 4-5, para. 8.) The specification provides a sound scientific basis to support grouping amphiphilic oligomers recited in claim 16. There is no suggestion in the record to suggest that the group is repugnant to scientific classification. Because *Harnisch* simply found that a group of compounds having a common structure and a common activity satisfies unity, unity exists if the compounds exhibit a common secondary and/or tertiary structure and a common activity. The compounds of claims 16-48 exhibit a common secondary and tertiary structure and thus satisfy the "common structure" test applied in *Harnisch*.

Accordingly, the compounds of claims 16-48 have two classes of common structures—a common repeating core structure and a common secondary and tertiary

structure. Each of these common structures satisfies one prong of the "unity of invention" test as applied in *Harnisch*.

(b) The Compounds of Claims 16-48 Have a Common Activity

In this case, not only do the compounds have a common structure, as recognized by *Harnisch* and shown above, they also meet the "common activity" prong of the test applied in *Harnisch*. *Harnisch,* 631 F.2d at 722. Claims 16-48 actually require the compounds to exhibit a common activity – antimicrobial activity. Specifically, claims 16-48 are directed to a method of treating a microbial infection in an animal in need thereof, comprising administering to the animal an effective amount of a pharmaceutical composition comprising an amphiphilic oligomer of Formula II. Therefore, claims 16-48 require that the compounds be effective in treating a microbial infection, and thus must exhibit the common antimicrobial activity.

Richard W. Scott, Ph.D., Vice President of Research at PolyMedix, confirms that compounds within the scope of claim 16's Markush expression have antimicrobial activity. According to Dr. Scott, in addition to the compounds having the common repeating core structure and also have a common amphiphilic structure, the compounds exhibit antimicrobial activity. (Exhibit F, p. 13, para. 13.)

Accordingly, the compounds of claims 16-48 exhibit a common activity, antimicrobial activity, which satisfies the second prong of the "unity of invention" test applied in *Harnisch*.

Because the compounds of claims 16-48 have both a common structure and common activity, then the compounds satisfy the unity of invention standard established by *Harnisch* for a proper Markush group.

***2. Claims 16-48 Possess Unity of Invention According to the Test Stated in* Hozumi**

Another test to determine whether a Markush group is proper is set forth in *Ex Parte Hozumi*, 3 U.S.P.Q.2d 1059, 1060 (Bd. Pat. App. Int. 1984). In *Hozumi*, the claimed

compounds were phosphoric acid diesters in which one esterifying moiety was derived from a poly(ethylene glycol) monoether and the other was derived from a beta-aminoethanol. *Id.* The claimed compounds were alleged to have antimycotic activity. *Id.* The Board interpreted the test set forth in *Harnisch* as requiring the compounds of the claims to have "in common a functional utility related to a substantial, structural feature disclosed as being essential to that utility." *Id.* Although this test is not the holding of *Harnisch*, *see Harnisch*, 631 F.2d at 722, nevertheless, for our purposes, claims 16-48 meet this test as well. The compounds of claims 16-48 have a functional utility related to a substantial, structural feature essential to that utility. The compounds utilized in the methods of claims 16-48 have antimicrobial activity. Further, the compounds utilized in the methods of claims 16-48 have a common repeating core structure, as well as a common secondary and tertiary structure.

Thus, the genus of compounds in claims 16-48 satisfies the test for a proper Markush group, as stated in *Hozumi*.

3. Claims 16-48 have Unity of Invention Under the PCT Test

A third test, not articulated by the Board in the Order, but capable of satisfying the "not repugnant to scientific classification holding" of *Harnisch* is the Patent Cooperation Treaty ("PCT") "unity of invention" standard. The American Bar Association and the American Intellectual Property Law Association recently proposed applying this standard to Markush claims. (Exhibits H & I.) This standard is explained in Chapter 10 of the PCT Examination Guidelines. (Exhibit J.)

"[U]nity of invention exists only when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding special technical features." (Exhibit J, p. 75.) "Special technical features" means "those technical features that define a contribution which each of the inventions, considered as a whole, makes over the prior art." (*Id.*) "Whether or not any particular technical feature makes a 'contribution' over the prior art, and therefore constitutes a 'special technical feature,' is considered with respect to novelty and inventive step." (*Id.*) "If the common matter of the independent claims is well known and the remaining subject matter of each claim differs from that of the

others without there being any unifying novel inventive concept common to all, then clearly there is lack of unity of invention." (*Id.*) However, if "there is a single general inventive concept that appears novel and involves inventive step, then objection of lack of unity does not arise." (*Id.*)

The PCT Examination Guidelines stress that "rigid rules cannot be given and each case is considered on its merits, the benefit of any doubt being given to the applicant." (*Id.*) Furthermore, the searching authority "should not raise objection of lack of unity of invention merely because the inventions claimed are classified in separate classification groups or merely for the purpose of restricting the international search to certain classification groups." (*Id.* at pp. 75-76.)

The PCT's "unity of invention" also applies to Markush practice. (*Id.* at p. 78.) "[T]he requirement of a technical interrelationship and the same or corresponding special technical features [defined above], is considered met when the alternatives are of a similar nature." (*Id.*)

> When the Markush grouping is for alternatives of chemical compounds, they are regarded as being of a similar nature where the following criteria are fulfilled: (A) all alternatives have a common property or activity, and (B)(1) a common structure is present, that is a significant structural element is shared by all of the alternatives, or (B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

(*Id.* at pp. 78-79.)

The compounds of claims 16-48 have a common property—antimicrobial activity. Moreover, as described above, the compounds utilized in the methods of claims 16-48 have a common repeating core structure, as well as a common secondary and tertiary structure. Therefore, the claimed compounds have a common property, antimicrobial activity, and a shared significant structural element.

Furthermore, claims 16-48 differ from the claim described in Example 24 of the PCT Examination Guidelines. The claim of Example 24 recites a compound of a formula, A-B-C-D-E. The definitions of A, B, C, D, and E in the Example 24 claim each encompass widely differing substituent groups. For example, A can be a saturated carbon chain, an unsaturated carbon chain, an aromatic ring, or a non-aromatic ring structure; B can be a saturated carbon chain, an unsaturated carbon chain, an amino, a sulfoxy, an ether, or a thioether; and C can be a non-aromatic ring or an aromatic ring. Therefore, just the A-B-C group of the compound can vary widely (*e.g.*, can be a saturated carbon chain-aromatic ring-nonaromatic ring, an aromatic ring-amino-aromatic ring, or an unsaturated carbon chain-ether-aromatic ring) and thus not form a common core structure. Because the claim encompasses a compound of formula A-B-C-D-E, the number of possible arrangements of defined groups varies widely and not form a common core structure.

Although the Example 24 claim appears to resemble Formula II of claims 16-48, the compounds of claims 16-48 share a common repeating structure unlike the Example 24 claim. Accordingly, claims 16-48, unlike Example 24, satisfies the PCT unity of invention standard.

Thus, for at least this reason, the genus of compounds in claims 16-48 satisfies the unity of invention test for a proper Markush group set forth in the PCT guidelines.

C. Public Policy Weighs in Favor of Not Restricting Within Claim 16 or Rejecting Claims 16-48 for Including Improper Markush Groups

1. If An Examiner Could Restrict Within a Claim, the Effect Would Decrease the Value of Applicants' Invention

In *Weber*, the CCPA recognized the general proposition that an applicant has a right to have each claim examined on the merits. *Weber*, 580 F.2d at 458. The CCPA found that if an examiner could restrict within a claim, forcing a single claim to be divided and presented in several applications, "that claim would never be considered on the merits," a potentially disastrous outcome in which the "the resulting fragmentary claims would not necessarily be the equivalent of the original claim." *Id.*

For example, a generic claim may encompass multiple subgenera or species. (Exhibit K, p. 6.) However, the specification may not provide written support for each and every subgenera or species. (*Id.*) If not, applicants could not pursue the subgenera or species as defined by the examiner in one or more subsequently filed applications. (*Id.* at p. 7.) Thus, applicants would not have patent coverage for that specific subgenera or species, even though the original generic claim would have provided such coverage.

Generic patent protection for a basic invention is fundamental for universities, as well as small research organizations. (Exhibit K, p. 8.) Scientists at universities often make pioneering discoveries which the universities then patent. (Exhibit L, p. 4.) A pharmaceutical company may then license the university-owned technology. (Exhibit K, p. 8.) The pharmaceutical company then will make and test new compounds within the scope of the generic claims. (*Id.*) Once the pharmaceutical company identifies the most efficacious compound, the pharmaceutical company will file an application with claims drawn to that specific compound. (*Id.*) If the university is unable to obtain a broad patent scope, the university will have disclosed, but not patented, compounds that fall within the originally filed genus. (*Id.* at p. 9.) Therefore, because companies wish to maximize profits by minimizing competition, a pharmaceutical company would be hesitant to license a patent with claims directed to a only a subgenus of these fundamental discoveries, but which discloses a multitude of unprotected compounds that could then be tested and marketed by a competitor. (*Id.*; Exhibit L, p. 4.)

Dr. Richard W. Scott, Ph.D., Vice President of Research at PolyMedix, confirms that in his experience, broad claims are valuable to both universities and small companies seeking investors. (Exhibit F, pp. 13-14, paras. 18-20.) Dr. Scott states that "inventors affiliated with universities often develop and patent cutting-edge technologies with broad application." (*Id.*) These pioneering inventions are then licensed to companies, such as start-up companies, which invest the resources to commercially develop the technology. (*Id.*, p. 13, para. 18.)

Dr. Scott states that without broad patent coverage, companies, such as start-up companies, will have fewer incentives to license pioneering inventions from universities. (*Id.*, pp. 13-11, paras. 18-20.) Therefore, without broad patent coverage, pioneering platform technology conceived by university-affiliated inventors may never be developed or marketed. (*Id.*)

Dr. Scott states that broad patent coverage is important to investors. (*Id.*) Additionally, Dr. Scott indicates that because of the time and expense necessary to investigate and identify lead compounds, a company requires assurance that it has broad patent coverage. (*Id.*, p. 14, paras. 19-20.) Furthermore, according to Dr. Scott, a broad intellectual property basis is important to protect a company's developing product line from look-alike products that share the overall design principles, but differ in specific, possibly insignificant, features. Without this level of protection, investors are wary to participate from fear in losing their investment to follow-on companies that have exploited the company's groundbreaking technology by finding gaps in its intellectual property. (*Id.*) Therefore, without broad patent protection, a start-up biotechnology company may find it impossible to obtain financing and thus be unable to develop and market products from pioneering inventions. (*Id.*)

PolyMedix was founded to commercialize the amphiphilic oligomer and polymer inventions of Drs. DeGrado, Klein, Tew, and others. (*Id.*, p. 2, para. 4; & p. 13, para. 18b.) These pioneering inventions occurred in the context of university research at University of Pennsylvania. (*Id.*) UPenn filed patent applications with claims encompassing the pioneering inventions of Drs. DeGrado, Klein, Tew, and others, including this application. (*Id.*, p. 2, para. 5.) The technology was exclusively licensed to PolyMedix, a start-up company, by UPenn. (*Id.*) PolyMedix is currently identifying lead compounds to develop and market as pharmaceutical compounds. (*Id.*, pp. 3-4, paras. 6-7; p. 11, para. 14; p. 13, para. 18b; & p. 14, para. 20.) Because UPenn has licensed this technology to PolyMedix, for the reasons described above, broad patent scope is vital to both UPenn and PolyMedix.

Accordingly, if the Office allows an examiner to restrict within a claim for administrative convenience and requires applicants to attempt to pursue each group in a separate application, applicants lose valuable statutory intellectual property rights.

2. An Examiner Could Restrict a Claim in Which the Groups Lack Written Description

If an examiner is allowed to restrict within a single claim, the examiner could define the groups in a manner that lacks written description in the specification. The CCPA considered this proposition in *Weber* when it held that the Office did not have the power to reject a claim under Section 121. *Weber*, 580 F.2d at 458. Specifically, the CCPA stated that "since the subgenera would be defined by the examiner rather than by applicant, it is not inconceivable that a number of the fragments would not be described in the specification." *Id.* (citing *Fields v. Conover*, 443 F.2d 1386 (1971) ("wherein a subgenus was not described") and *In re Ruschig*, 379 F.2d 990 (1967) ("wherein a species of a properly described genus was found not to be described.")) If the examiner does define the groups in a manner that lacks written description in the specification, then newly presented claims would be invalid under 35 U.S.C. § 112, first paragraph, or violate 35 U.S.C. § 132's prohibition on new matter.

In the present application, the Examiner issued a 28-way restriction requirement. (Restriction Requirement, September 6, 2006, pp. 2-5.) In the restriction requirement, none of the groups provided by the Examiner actually read on any compound disclosed in the specification, much less the compound the Applicants elected in the response filed June 12, 2006. (Amendment and Reply, October 24, 2006, pp. 51-54.) As a result, the Applicants were unable to select a group for further prosecution. (*Id.*)

By having to reply to a restriction requirement that divided the claim in a manner that did not adhere to the description of the invention, prosecution was delayed and additional costs were accrued.

Accordingly, if an examiner is allowed to restrict within a claim, applicants' resources may be wasted in responding to a restriction requirement in which the claim is divided in a manner that lacks or possess tenuous written description support.

3. Restricting Within a Claim Would Lead to Increased Costs

If an examiner is allowed to restrict within a single claim, the costs incurred by applicants and the Office would increase. For example, because developing a commercial pharmaceutical product is a long process, the inventors often do not know which compounds ultimately will be pursued in clinical trials at the time a restriction requirement is issued. If an examiner restricts within a single claim, applicants will be faced with having to file multiple applications to obtain the original patent coverage. (Exhibit L, p. 5.) The costs associated with filing these additional applications, including Office administrative fees, as well as attorney fees, may be very high and thus have a negative impact on budgets. (*Id.*) Because additional applications will have a negative impact on budgets, companies will likely discard valuable species during the investigative stages, making development of useful products less likely. (*Id.*)

Additionally, the Office will incur increased costs if an examiner is allowed to restrict within a single claim. For example, large number of additional divisional applications may increase the backlog at the Office, rather than decreasing the backlog. (*Id.*) To address the increasing backlog of pending applications, the Office may be required to hire additional examiners.

Accordingly, if an examiner is allowed to restrict within a claim, costs to the applicants and the Office would increase.

V. Conclusion With Respect to the Markush Group Questions

The Office has no authority to restrict within a single Markush claim. The Board has no statutory authority to issue such a rule. Furthermore, as described above, even if the Office has such authority, there is no *per se* test to be applied to determine unity of invention. Instead, the test is fact-specific and is to be applied on a case-by-case basis. In

this case, the compounds of claims 16-48 meet the commonly applied tests used to determine unity of invention. Finally, as described herein, there is sound public policy behind allowing applicants to set forth the metes and bounds of what they regard as their invention, not the Office; especially for the type of pioneering invention set forth in the present application.

CONCLUSION

For the reasons discussed above regarding the Section 121 questions Applicants have demonstrated that (1) the Board has no jurisdiction to review restriction requirements in this case; (2) there is no conflict between Section 121 and the holdings in the *Weber* and *Haas* cases; and (3) the second paragraph of Section 112, in addition to the plain language of Section 121, does not allow the Director any discretion to require a restriction within a claim.

Additionally, for the reasons discussed above regarding the Markush questions, Applicants have demonstrated that (1) the Office has no statutory basis for rejecting a claim for containing an improper Markush group; (2) there is no *per se* rule to apply when determining a proper Markush group; and (3) claims 16-48 of the application contain proper Markush groups because the groups possess unity of invention under any test applied by the Board.

Accordingly, Applicants respectfully request that the Board address the issue on appeal, that the rejection of pending claims 16-48 and 67-73 under the judicially created doctrine of obviousness-type double patenting is in error and should be reversed. Thus, Applicants request that the Board allow these claims be allowed to issue.

Respectfully submitted,

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EVIDENCE APPENDIX[3]

Exhibit A	U.S. Patent No. 7,678,801
Exhibit B	U.S. Patent No. 7,825,216
Exhibit C	U.S. Patent No. 7,897,596
Exhibit D	U.S. Patent No. 7,932,242
Exhibit E	U.S. Patent No. 7,939,553
Exhibit F	Declaration of Richard W. Scott, Ph.D. Under 37 C.F.R. § 1.132
Exhibit G	Considine, D.M., ed, *Van Nostrand's Scientific Encyclopedia*, 8th ed., p. 226, Van Nostrand Reinhold, New York, NY (1995)
Exhibit H	Jenkins, M., American Bar Association Comments on Proposed Changes to Restriction Practice in Patent Applications, (August 11, 2010)
Exhibit I	Kirk, M.K., American Intellectual Property Law Association Response to Notice Requesting Comments on Proposed Changes to Restriction Practice in Patent Applications, (August 13, 2010)
Exhibit J	PCT Examination Guidelines, Chapter 10 – Unity of Invention
Exhibit K	Testimony of H.C. Wegner in response to Proposed Rulemaking, "Examination of patent applications that include claims containing alternative language", pp. 1-18 (August 10, 2007)
Exhibit L	Comments of the Biotechnology Industry Organization on the United States Patent & Trademark Office Proposed Rule Changes Concerning Claims Containing Alternative Language (October 9, 2007)

3 Applicants have concurrently filed the necessary petitions to enter this new evidence and supplemental material into the record.